Ultrasound in Med. & Biol., Vol. 35, No. 9, pp. 1488–1501, 2009

0301-5629/09/$–see front matter

ELSEVIER

doi:10.1016/j.ultrasmedbio.2009.04.007

● *Original Contribution*

TWO-DIMENSIONAL STRAIN IMAGING OF CONTROLLED RABBIT HEARTS

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(*Received* 16 *April* 2008, *revised* 20 *March* 2009, *in final form* 8 *April* 2009)

Abstract—Ultrasound strain imaging using 2-D speckle tracking has been proposed to quantitatively assess changes in myocardial contractility caused by ischemia. Its performance must be demonstrated in a controlled model system as a step toward routine clinical application. In this study, a well-controlled 2-D cardiac elasticity imaging technique was developed using two coplanar and orthogonal linear probes simultaneously imaging an isolated retroperfused rabbit heart. Acute ischemia was generated by left anterior descending (LAD) artery ligation. An excitation-contraction decoupler, 2,3-butanedione monoxime, was applied at a 4-mM concentration to reversibly reduce myocardial contractility. Results using a single probe demonstrate that directional changes in the in-plane principal deformation axes can help locate the bulging area as a result of LAD ligation, which matched well with corresponding Evans Blue staining, and strains or strain magnitude, based on principal stretches, can characterize heart muscle contractility. These two findings using asymmetric displacement accuracy (*i.e.*, normal single-probe measurements with good axial but poor lateral estimates) were further validated using symmetric displacement accuracy (*i.e.*, dual-probe measurements using only accurate axial tracking estimates from each). However, the accuracy of 2-D cardiac strain imaging using a single probe depends on the probe's orientation because of the large variance in lateral displacement estimates. (E-mail: cxjia@umich.edu) © 2009 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Cardiac strain, 2-D Speckle tracking, Principal stretch, Langendorff.**

INTRODUCTION

Myocardial ischemia and infarction because of the occlusion of coronary arteries alter the contractility of cardiac muscle, producing segmental akinesis or systolic bulging (dyskinesis) (Akaishi et al. 1986; Holmes et al. 2005). This regional wall motion abnormality has become one of the key indicators for visual interpretation and diagnosis of heart disease using echocardiography (Heger et al. 1979). However, this method is observer dependent (Thomas and Popovic 2006).

Ultrasound strain and strain rate imaging have been proposed to quantitatively assess regional myocardial deformation (D'hooge et al. 2002; Kaluzynski et al. 2001; Uematsu et al. 1995; Urheim et al. 2000). Doppler tissue imaging (DTI)–derived elasticity imaging (D'hooge et al. 2002; Uematsu et al. 1995; Urheim et al. 2000) and correlation-based 2-D speckle tracking (Kaluzynski et al. 2001; Lee et al. 2007; Leitman et al. 2004; Notomi et al. 2005) are two major ultrasound techniques to measure myocardial strain (D'hooge et al. 2000; Thomas and Popovic 2006).

DTI-derived strain imaging has been investigated in phantom experiments (Matre et al. 2003), animal experiments (Urheim et al. 2000) and human experiments (Edvardsen et al. 2002; Pellerin et al. 2003), demonstrating the feasibility of clinical application (Sutherland et al. 2004). However, these methods are severely limited by angle dependency because only one component of the symmetric strain tensor (3 and 6 components in 2-D and 3-D tensors, respectively) can be measured along the

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beam direction (D'hooge et al. 2000; Edvardsen et al. 2002; Thomas and Popovic 2006). The second limitation is that DTI-derived strain estimates suffer from low signal-to-noise ratio (SNR) (Chen et al. 2005; Hanekom et al. 2007) because relatively high repetition frequencies are required to minimize decorrelation because of multidimensional motion. Axial displacement images estimated using DTI-derived methods are visually noisier than those using phase-sensitive 2-D speckle tracking (Chen et al. 2005).

An alternative approach to strain imaging using 2-D non-Doppler speckle tracking can minimize the angle dependency problems of Doppler-based methods by estimating in-plane 2-D strain components. Non-Doppler speckle tracking can be divided into two categories according to different input data: phase-insensitive speckle tracking using B-mode gray-scale images (Leitman et al. 2004; Migrino et al. 2007) and phase-sensitive speckle tracking using radiofrequency (RF) data (Brusseau et al. 2008; D'hooge et al. 2002; Kaluzynski et al. 2001; Konofagou and Ophir 1998; Lee et al. 2007; Lopata et al. 2006; Maurice and Bertrand 1999). Phase-insensitive 2-D tracking has poor precision in both dimensions, whereas phase-sensitive tracking has good precision along the propagation direction and relatively poor precision orthogonal to the propagation direction (Lubinski et al. 1999).

It has been shown that phase-insensitive tracking can overcome Doppler-based, DTI-derived strain imaging's angle dependence in animal experiments (Migrino et al. 2007; Rappaport et al. 2008) and clinical patient investigations (Cho et al. 2006; Leitman et al. 2004; Perk et al. 2007). Without phase information, however, the results depend highly on spatial and temporal smoothing, and traces of strain components only represent the overall behavior of large segments.

In contrast, phase-sensitive speckle tracking using RF images can refine tracking results along the propagation direction using the calculated phase zero–crossing position (Lubinski et al. 1999), and this improvement in one direction leads to higher accuracy in the accumulated results in both directions (see section on 2-D speckle tracking under Materials and Methods). Therefore, phase-sensitive speckle tracking not only can overcome the angle limitation of Doppler-based methods, but can also provide more accurate results, with higher spatial resolution for each strain component, an important feature to derive coordinate-independent principal axes and strains based on the principal stretches along these axes. The accuracy and higher spatial resolution is valuable to detect the transmurality of myocardial ischemia or infarction. In this study, phase-sensitive speckle tracking is used to estimate myocardial deformation.

In continuum mechanics, deformation at one point in a solid body can be fully characterized by strains based on the principal stretches along the principal axes, where a proper coordinate rotation is applied to eliminate all shear components (Atkin and Fox 1980). These parameters are only related to the deformation status at that point and are theoretically independent of coordinates. In this study, we propose to use in-plane strains based on the principal stretches along the principal axes to characterize the contractility of heart muscle and the directional change of the principal axes to detect abnormal motion. In the remainder of this paper, we will often refer to deformation estimated in this way simply as strains.

Note that strains (Chen 2004; Jia et al. 2007) obtained by deriving the principal stretches from the right Cauchy deformation tensor are different from the principal strains (Zervantonakis et al. 2007) calculated using the finite Lagrange deformation tensor. The latter includes a second-order term in the fractional deformation, where the former is more precise and direct when estimating the fractional deformation compared with the original length in large strain situations, such as the accumulated deformation at the end of the systole, as shown in the Appendix.

Estimation of strains based on principal stretches and their principal axes is independent of the coordinate system or the orientation of the probe. These strains are derived from the eigenvalues and eigenvectors of the right Cauchy deformation tensor. The tensor captures the deformation status at that point and that moment regardless of the probe's orientation. However, the accuracy and precision of estimated strains and their principal axes depend on the probe's orientation. Because displacements used to estimate the right Cauchy deformation tensor are estimated by multidimensional, phase-sensitive speckle tracking, they exhibit higher variance in the lateral direction than the axial direction because of the availability of phase information only along the ultrasound propagation direction (Lubinski et al. 1996). The unequal estimation variances between displacements along the beam and those perpendicular to it lead to the unequal estimation variances of the components in the right Cauchy deformation tensor. Therefore, the accuracy and precision of estimated strains and their principal axes derived from the right Cauchy deformation tensor depend on the direction of ultrasound propagation relative to the principal axes.

In this paper, we describe a well-controlled *in vitro* experiment on an isolated rabbit heart paced from the apex. Two coplanar and orthogonal linear probes were used to acquire RF data. Left ventricle (LV) pressure and electrocardiogram (ECG) signals were recorded and synchronized with ultrasound RF data acquisition using a field programmable gate array (FPGA). Acute ischemia was generated by ligating the left anterior descending (LAD) coronary artery on an isolated Langendorff retro-perfused rabbit heart. Results from a single probe show that systolic bulging of the heart wall because of LAD ligation can be detected by significant directional changes